Docket No.: LUD 5501.1 CON. US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jean-Christophe Renauld

Application No.: Not yet assigned

Group Art Unit: N/A

Filed: Concurrently herewith

Examiner: N/A

For: ASTHMA ASSOCIATED FACTORS AS TARGETS FOR TREATING ATOPIC ALLERGIES INCLUDING ASTHMA AND RELATED DISORDERS

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, DC 20231

Sir:

Prior to Examination please amend the application as follows:

IN THE SPECIFICATION

Page 6, please delete line 31, beginning "Figure 2:..." and insert therefore

- -Figure 2: Alignment of the murine M-Ras protein (SEQ ID NO:1) with p21 H-Ras (SEQ ID NO: 16) and R-Ras (SEQ ID NO: 17).- -

On page 1, delete lines 4 and 5 and insert the following replacement lines:

- -This application is a continuation of U.S. Application No. 09/157,247 which claims the benefit of U.S. Provisional Patent

Application Serial No. 60/059,509 which was filed September 19, 1997. This invention is also related to the subject- -

On page 20 please delete the paragraph between lines 22 and 30 and insert therefore the following paragraph:

- -In still another aspect of the invention. surprisingly, aminosterol compounds were found to be useful in the inhibition of M-Ras induction by mitogen stimulation. Aminosterol compounds which are useful in this invention are described in the following U.S. Patents: 5,637,691; 5,733,899; 5,721,226; 5,840,740; 5,795,885; 5,994,336; 5,763,430, and; 5,840,936, which are specifically incorporated herein by reference. The ability of an aminosterol compound to block M-Ras induction could be determined by any one of numerous assays previously described in the art which screen for signaling partners of Ras proteins (Kimmelman et al., 1997; Vojtek et al., 1993). - -

Page 36, please delete the two first paragraphs, lines 1-6, and insert therefore:

- - Nucleic acid molecules comprising the following sequences hybridize to probe comprising SEQ ID NO: 1 under the above conditions: 5' - CAGACTGGCACAGTTCC-3' (SEQ ID NO: 12) and 5'-TGCTGTAGAAGCCGAAGCC-3' (SEQ ID No: 13).

Nucleic acid molecules comprising the following sequences hybridize to probe comprising SEQ ID NO: 3 under the above stringent conditions: 5'-GAATTCAGCGCCATGCGC-3' (SEQ ID NO: 14) and 5'-CCTCACAAGATCACACATTG-3' (SEQ ID NO: 15).- -

Please add the attached Sequence Listing to the application.

IN THE CLAIMS

Please cancel claims 1-37, 41-43, 45-48 and 51-52 without prejudice.

Please amend the following claims:

38. A method of quantifying a M-Ras polypeptide of claim 58 comprising the steps of:

(a) contacting a sample suspected of containing M-Ras polypeptide with an antibody that specifically binds to the M-Ras polypeptide under conditions that allow for the formation of reaction complexes comprising the antibody and M-Ras polypeptide; and

(b) detecting the formation of reaction complexes comprising the antibody and M-Ras polypeptide in the sample,

wherein quantitation of the reaction complexes indicates the level of M-Ras polypeptide in the sample.

Please add the following claims:

- -53. An isolated nucleic acid molecule encoding an M-Ras polypeptide that is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 3.

54. The isolated nucleic acid molecule of claim 53, wherein said nucleic acid molecule is a cDNA.

55. The isolated nucleic acid molecule of claim 53, wherein said nucleic acid molecule is a genomic DNA.

56. The isolated nucleic acid molecule of claim 53 wherein said nucleic acid molecule is an mRNA.

57. The isolated nucleic acid molecule of claim 53 wherein said nucleic acid molecule consists of a nucleotide sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 3.

58. An isolated polypeptide encoded by the isolated nucleic acid molecule of claim 53.

59. A method for detecting or diagnosing susceptibility to a pathologic condition associated with expression of M-Ras in a human subject comprising

(a) measuring the level of M-Ras polypeptide in a biological sample from a human subject suspected of having said pathologic condition or being susceptible to said pathologic condition, and

(b) comparing the level of M-Ras polypeptide present in normal subjects,

wherein an increase in the level of M-Ras polypeptide in the biological sample from said human subject as compared to levels of said M-Ras polypeptide in normal subjects is indicative of said pathologic condition or indicative of a susceptibility to said pathologic condition..

60. A method for monitoring the therapeutic treatment of a pathologic condition associated with expression of M-Ras comprising measuring the levels of M-Ras polypeptide in a series of biologic samples obtained at different time points from a subject undergoing a therapeutic treatment wherein a significant decrease is said levels of M-Ras polypeptide indicates a successful therapeutic treatment.

61. A method for the therapeutic treatment of a pathological condition associated with expression of M-Ras comprising administering an effective amount of a compound to down-regulate M-Ras function wherein said amount is sufficient to treat the pathological condition.

62. The method of claim 61, wherein said compound is selected from the group consisting of farnyesyl transferase inhibitor, manumycin A, lovastatin, geranylgeranyl transferase

inhibitor, an inhibitor of the MAPK pathway, an antisense DNA complementary to SEQ ID NO: 1, and an antisense DNA complementary to SEQ ID NO: 3.

63. The method of claim 61, wherein said pathologic condition is selected from the group consisting of an asthma-related disorder, a lymphoma, a leukemia and Mycosis fungoides.

64. A method for preparing an antibody specific for an M-Ras polypeptide encoded by the nucleic acid molecule of claim 53, comprising

(a) conjugating said M-Ras polypeptide, or fragments thereof containing at least 10 contiguous amino acids of said M-Ras polypeptide, to a carrier protein,

(b) immunizing a host animal with said conjugate admixed with an adjuvant, and

(c) obtaining antibody from said host animal.

65. An isolated antibody specific for the polypeptide encoded by the nucleic acid molecule of claim 53.

66. The isolated antibody of claim 53, wherein said antibody is a monoclonal antibody.

67. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of (a) SEQ ID NO: 2, wherein residue 22 of SEQ ID NO: 2 is a valine, (b) SEQ ID NO: 4, wherein residue 22 of SEQ ID NO: 4 is a valine, (c) SEQ ID NO: 2, wherein residue 71 of SEQ ID NO: 22 is a lysine, (d) SEQ ID NO: 4, wherein residue 71 of SEQ ID NO: 2 is a lysine, (e) SEQ ID NO: 2, wherein residue 22 is a lysine and (f) SEQ ID NO: 4 wherein residue 22 is a lysine.

68. An isolated nucleic acid molecule which has a nucleotide sequence that is complementary to the sequence of the nucleic acid molecule of claim 53.

69. The nucleic acid molecule of claim 68, wherein said nucleic acid molecule is an antisense DNA molecule.

70. The isolated nucleic acid molecule of claim 49, wherein said nucleic acid molecule is an mRNA.

71. The isolated nucleic acid molecule of claim 53, wherein said nucleic acid molecule consists of a sequence set forth in SEQ ID NO: 1 or SEQ ID NO: 3. - -

REMARKS

Applicants have canceled claims 1-37, 41-43, 45-48 and 51-52 without prejudice and expressly reserving the right to pursue any of the subject matter of these claims in one or more subsequent applications.

Applicants have added claims 53-71, which are essentially a consolidation of the original claims. Support for the added claims is found in the original claims as filed and throughout the specification.

Applicants respectfully request that the foregoing amendments be entered into this application.

The Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 06-2375.

Respectfully submitted,

Date: Feb. 8, 2002

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Version of claims and specification paragraphs with amendments indicated

deletions bracketed, insertions underlined

38. A method of quantifying a M-Ras polypeptide of claim [8 or 9] 58 comprising the steps of:

(a) contacting a sample suspected of containing M-Ras polypeptide with an antibody that specifically binds to the M-Ras polypeptide under conditions that allow for the formation of reaction complexes comprising the antibody and M-Ras polypeptide; and

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